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Giant Cell Tumor of the Tendon Sheath: A Retrospective Study of 28 Cases

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Background and Objectives: Giant cell tumor of the tendon sheath (GCTTS) is a lesion of uncertain etiology. To better interpret pathogenesis and aid in the differentiation of GCTTS from other similar pathological processes we reviewed the literature and analyzed the available information.

Methods: We retrospectively studied clinicopathologic findings in 28 cases of GCTTS on the basis of anatomic location and histologic appearance of the lesion.

Results: The GCTTS could be divided into those involving the common digits (20 cases) and larger joint group (8 cases) based on anatomic location. Grossly the digit tumors were small, multiple, surrounded by a thin fibrous capsule, and had a variegated appearance, while the large joint tumors were relatively large and covered by one or more layers of synovium. Microscopically both groups consisted of a mixture of round to polygonal histiocytes, foam cells, hemosiderin laden macrophages, and multinucleated giant cells. The giant cells seemed more abundant in the digit tumors, while the pseudoglandular spaces lined by synovial cells were more striking in the large joint group.

Conclusions: Local excision was the treatment of choice in the majority of the patients. Eight patients had local recurrence.

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KEY WORDS: **giant cell tumors; tendon sheath; small joint tumors; digit tumors; large joint tumors**

INTRODUCTION

In the pathologist's world of cells, giant cells crop up in numerous unexpected disease states. One such giant cell rich tumor which deserves a second look, because it has a potential for mischief and mimicry, is the giant cell tumor of the tendon sheath (GCTTS). A number of benign tumors or tumor-like lesions arise from the synovium, yet only the giant cell tumor is considered prototypical [1].

The GCTTS is recognized by a plethora of names that generally reflects the polymorphic nature of its tissue components. In the past, this lesion has been variously described as fibrous xanthoma, benign synovioma, sclerosing hemangioma, and GCTTS [2,3]. Jaffe et al. [2] in 1941 concluded that all these lesions were in reality part of a common family and the differences in clinical extent and growth were influenced by anatomical location. They grouped them under the term pigmented villonodular synovitis or nodular tenosynovitis. Since then it has been studied by many investigators but confusion still exists as to its nature. Several authors have speculated about the etiology as certain features of the lesion suggest trauma or inflammation while others imply metabolic disease or neoplasia [2].

We describe here the clinicopathologic findings of 28 cases of GCTTS on the basis of anatomic location and histologic appearance of the lesion with a review of the literature and analysis of available information in order to better interpret pathogenesis and aid in the differentiation from other similar pathological processes.

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TABLE I. Age Ranges of the 28 Patients With GCTTS

Age range (years)	No. of cases
0–9	1
10–19	2
20–29	6
30–39	9
40–49	5
50–59	3
60–69	2

MATERIALS AND METHODS

The clinical records of all patients attending Tata Memorial Hospital who had had a pathological diagnosis of GCTTS over a period of 10 years from 1980 to 1990 were reviewed. All cases of GCTTS arising from areas where the synovium is normally found were included, except cases of direct malignancy and giant cell tumor of bone.

The hematoxylin-eosin (H&E)-stained microscopic slides were reviewed. The paraffin blocks were available in all cases and fresh sections (5 μm thick) were cut and stained with H&E. Roentgenograms were reviewed in cases where they were available. Follow-up data were obtained from clinical records and from letters of inquiry.

RESULTS

Clinical Features

Ages of patients ranged from 8 to 69 years with most cases occurring in the third decade (Table I). There was a female predominance of 10 males to 18 females. The majority of patients complained of a painless, palpable mass which gradually increased in size. Tenderness or dull pain occurred in six cases. History of antecedent trauma was present in six cases. The duration of symptoms recorded ranged from 6 weeks to 3 years with an average duration of 6 months.

Examination and Treatment

On the basis of anatomical location, these lesions were divided into small joint, localized type (20 cases) and large joint, diffuse type (8 cases). The majority of small joint tumors occurred in the digits, especially the fingers, more commonly on the index finger of the right hand (five cases) (Table II). The digit tumors were soft to firm in consistency, non-tender, multinodular, and fixed to deep structures but not attached to the skin. The gliding of the tendon was not affected significantly. The anatomic distribution of tumors of the diffuse type is shown in Table III. The joints adjacent to or involved by the lesion were the knee joint, ankle-foot, wrist, and elbow in descending order of frequency. The swelling was usually diffuse and painful. The joint movements were affected in four cases.

Preoperative X-ray films were available in six cases and showed bone erosion in two cases, cystic degenerative change in one case, and soft tissue swelling with cortical erosion in two cases involving the large joints. No abnormality was detected in one case.

TABLE II. Anatomic Location of Small Joint Tumors (20 Cases)

Site	Right	Left	Unknown	Total
Fingers				
Thumb	2	2	1	5
Index	5	1	1	7
Middle	1	1	—	2
Ring	1	1	—	2
Little	1	—	—	1
Toes				
1st	2	—	—	2
2nd	—	—	—	—
3rd	—	1	—	1
4th	—	—	—	—
5th	—	—	—	

TABLE III. Anatomic Location of Large Joint Tumors (8 Cases)

Site	Right	Left	Unknown	Total
Ankle-foot	1	1	—	2
Knee	2	1	1	4
Wrist	1	—	—	1
Elbow	1	—	—	1

Excision was the treatment in most of the cases. Although most patients were lost to follow-up, eight patients had local recurrences which were benign, with one case recurring repeatedly until amputation of the digit.

Pathologic Features

Gross examination. The tumors in the small joint group were well-circumscribed, encapsulated masses with smooth but lobulated contour, varying in size from 0.5 to 3 cm at the greatest diameter (average size 1.5 cm). Cut section of the tumor was gray-white mottled with pink, brown, or yellow. The large joint tumors were more irregular in shape, ranging in size from 1.5 to 5.5 cm (average size 3 cm). The nodules were firm and usually unencapsulated. Cut section was grayish white.

Microscopic findings. The characteristic lobulation seen in the gross specimens was also visible microscopically. Although microscopic findings varied considerably in different tumors and even in different parts of the same tumor, the lesions of the localized and diffuse type were composed essentially of a single set or groups of rounded or polygonal cells having round nuclei and faintly eosinophilic cytoplasm interspersed amidst giant cells (Fig. 1). In some areas, the mononuclear cells had an elongated, somewhat spindled contour. These cellular areas were interspersed with sparsely cellular collagenous connective tissue dividing the lesion into lobules and forming a capsule in the small digit group. Foci of xanthomatous changes were seen. Hemosiderin granules were seen in

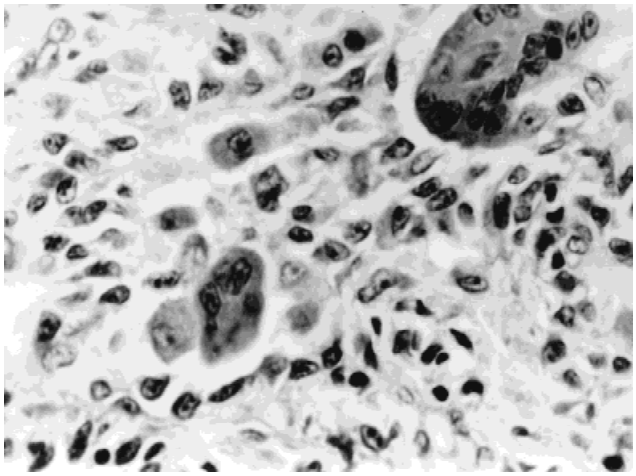

Fig. 1. Round or polygonal cells are seen interspersed amidst giant cells.

the cytoplasm of the stromal cells, especially the foam cells.

The giant cells had a deeply eosinophilic cytoplasm and contained a variable number of nuclei ranging from as few as 4 to as many as 60. No special arrangement of the nuclei within the cytoplasm was noted. The giant cells were irregularly distributed and appeared to be more numerous in the small digit group. The lesions were rich in vascular supply. Hemorrhage was seen in one case. A small number of synovial-lined clefts were seen in the digit group compared to the large joint lesions, which showed many cleft-like and pseudoglandular spaces lined by cuboidal to round cells.

Mitotic figures were seen in three cases. They varied in number from 2 to 4 per 10 high power fields (hpf). No atypical mitosis was seen. Inflammatory cells were sparse.

When fragments of synovium were included in the microscopic sections, the synovial tissue was usually normal or showed only slight thickening.

DISCUSSION

It was Jaffe and coworkers in 1941 [2] who regarded the synovium of the tendon sheath, bursa, and joint as an anatomical unit that could generate a family of lesions including the GCTTS (nodular tenosynovitis), localized and diffuse forms of pigmented villonodular synovitis, and extra-articular pigmented villonodular synovitis arising from bursae. Since then there have been reports about this lesion which further defined the entity [4–12].

GCTTS occurs in the tendon sheaths of digits or in joints of the extremities. The tumors of the digits grow in a narrow space, while those in large joints may expand. These circumferential factors seem to influence greatly the clinical as well as microscopic features.

Recognition of GCTTS in typical cases is not difficult from the clinicopathologic viewpoint, especially in the small digit lesions [1,6]. Seventy percent of our patients with small joint involvement had a painless subcutaneous nodular swelling which gradually increased in size. The joint was usually not involved. In the large joint group, which is rarer, it is difficult to detect unless the swelling is painful or the joint is involved, as occurred in six of our cases.

The peak incidence noted in the third decade with a female preponderance, the frequent involvement of the index finger among the small digit tumors and the right knee joint in the large joint group, and X-ray findings in our study agree with similar observations made in other published series [1–3,5,8,11,12].

Grossly the small digit lesions were encapsulated and were more yellow to brown on cut section than the large joint group which were unencapsulated and gray-white on cut section. Histologically, both the small and the large joint groups had a mixture of mononuclear cells, foam cells with hemosiderin granules, spindle cells, and giant cells interspersed with connective tissue. The differences noted histologically between the two groups were in the number of giant cells which were less in the large joint lesions and the presence of pseudoglandular spaces and synovial clefts in the large joint group. These histologic features were in keeping with the tabulated differences between the two groups suggested by Ushijima et al. [9].

The presence of mitotic figures in both the small and large joint groups has been documented [5,6,8,9]. Mitotic figures were noted in 11% of our cases. Rao and Vigorita [13] documented 3 or more mitotic figures per 10 hpf in 13% of their cases. No atypical mitosis has been noted. Although mitosis may indicate an actively growing lesion, there is no evidence to suggest that such lesions are malignant or prone to metastasis.

The etiology and cell of origin of these lesions have been debated and speculated about. Is it reactive or neoplastic? In favor of reactive etiology is the fact that a number of patients experience antecedent trauma [2,6,9]. In our study, 21% of patients had a past history of antecedent trauma. Also, the microscopic appearance of the synovium in degenerative joint disease, traumatic arthritis, and experimental synovitis produced by repeated hemarthroses is similar in some respect to nodular tenosynovitis [14]. Histologically, the cellular elements resemble histiocytes which have undergone metaplasis to give the other cell types noted [1]. Multinucleated giant cells are formed by fusion of histiocytes. Foam cells are seen in many chronic inflammatory conditions.

In favor of a neoplastic origin was the observation that all of these lesions are capable of a certain degree of autonomous growth with local recurrence which is affected by the clinical extent of the disease and surgical removal [1,4,9]. Also, exceedingly rare cases have been reported giving rise to metastatic disease [15]. The pres-

ence of an aneuploid DNA pattern and high proliferative index in some cases of diffuse GCTTS coupled with the reported chromosomal abnormalities and occurrence of malignant transformation in these lesions point to their neoplastic nature [16].

Enzyme histochemistry studies have shown positive results with acid phosphatase, non-specific esterase, and alpha-naphthyl butyrate esterase and beta glucuronidase which were demonstrated in the predominant cells thus confirming monocyte/macrophage lineage [9,10]. Alguacil-Garcia et al. [16] documented that by electron microscopy GCTTSs were seen to be composed of A and B type synovial cells and were reactive and borderline proliferative lesions. On the other hand, Carstens [8] believed that GCTTS was closely related to osteoblastic mesenchyme. Though the accurate histogenesis of the lesions is still obscure, Ushijima et al. [9] and Wood et al. [10] have concluded that both the mononuclear cell and giant cell of GCTTS exhibit the antigenic and enzymatic features of monocyte/macrophage, supporting the concept that GCTTSs are synovially derived only to the extent that GCTTSs may arise from cells of monocyte/macrophage lineage found within or lining synovial tissue. This was also proved by Athanasou et al. [17], who showed that GCTTS is composed of cells of histiocyte differentiation with the giant and mononuclear cell components expressing a similar cytogenic phenotype and that bone resorption by macrophage polykaryons shows that this is not a unique defining characteristic of osteoclasts. Comparing all the observations, the overall impression leads one to believe in the essentially benign nature of this condition.

On occasion, GCTTS may be confused with other lesions. The small digit lesions have to be differentiated from granulomatous lesions, necrobiotic granulomas, and multiple giant cell tumors with prominent xanthomatous component which usually arise in a setting of hyperlipemia and fibroma of the tendon sheath. A histological scoring system has been described for differentiating GCTTS from fibroma of the tendon sheath which is considered to be a part of the same family [18]. The differential diagnoses of large joint tumors include synovial sarcoma, rhabdomyosarcoma, and inflammatory or xanthomatous forms of malignant fibrous histiocytoma. Pigmented villonodular synovitis, which belongs to the same family, has to be differentiated from large joint GCTTS because of different treatment strategies. The distinguishing feature lies in the villous proliferation on the surface and large deposits of hemosiderin seen in pigmented villonodular synovitis. Malignant forms of GCTTS have also been recognized as distinct from synovial sarcoma [15,19].

The treatment of choice for GCTTS is local excision with a cuff of normal tissue without causing disability to the joint. Local recurrence has been noted in both small and large joint groups. In our study, recurrence rate was 28%, which is comparable with some studies [1,6]. A few reports have been noted with higher recurrence rates probably due to extended follow-up, incomplete excision, or residual satellite nodule [4,9].

CONCLUSIONS

A distinct histopathologic variation was noticed between GCTTS involving the digits and large joints. Early diagnosis and treatment with wide excision offer an excellent prognosis.

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